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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,772	06/15/2000	DEREK O'HAGAN	PP01388.202	7681

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 12/16/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/581,772

Applicant(s)

O'HAGAN ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7, 9-16, 43-47, 52-54, 56-59 and 69-90 is/are pending in the application.
- 4a) Of the above claim(s) 9, 52, 53 and 81-84 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-16, 43-47, 54, 56-59, 69-80, and 85-90 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Status of the Claims In the prior action mailed on April 24, 2002, claims 1-7, 9-19, and 21-68 were pending in the case, and claims 1-7, 10-16, 43-47, and 54-59 were under consideration and rejected. In the amendment filed by applicant on September 30, 2002 (Amend. B), claims 17-19, 21-42, 48-51, 55, and 60-68 were cancelled, claims 1-7, 9-12, 14-16, 43-47, 52-54, 56, and 57 were amended, and claims 69-90 were added.

Of the new claims, each of the claims 69- 80 and 85-90 read on both the elected invention and on non-elected inventions and are therefore under examination only to the extent that they read on the elected microparticles. Claims 81-84 read on non-elected embodiments and are therefore withdrawn from examination.

Currently claims 1-7, 9-16, 43-47, 52-54, 56-59, and 69-90 are pending. Claims 1-7, 10-16, 43-47, 54-59, 69- 80, and 85-90 are under consideration. Claims 9, 52, 53, and 81-84 are withdrawn from consideration as reading on non-elected inventions.

2. The Art Unit location of your application, and the examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

Information Disclosure Statement

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3. The information disclosure statement (IDS) submitted on contains reference to PCT publication WO 96/20698. This reference is already of record in the case. See, Form PTO 892, attached to paper 6. Therefore, the reference has been crossed out on the IDS disclosure. Because it is already of record, it has also been previously considered.

Specification

4. In the prior action, the specification was objected to for not containing an abstract. An abstract was added to the application in Amend. B. The objection is therefore withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(Prior Rejection-Withdrawn)** Claims 2, 3, 28, 44, and 45 were rejected in the prior action for containing reference to terms not defined in the specification, and therefore made the metes and bounds of the claim indeterminate. These terms have been removed from the claims (except for claim 28, which was cancelled). The rejection is therefore withdrawn.

7. **(Prior Rejection Withdrawn)** Claim 30 was rejected as indefinite for use of the term "gp120" without identifying what organism the antigen was associated with. The claim has been amended to identify the antigen. The rejection is therefore withdrawn.

8. **(Prior Rejection- Withdrawn)** Claim 15 was rejected for indefiniteness in the prior action for not identifying what the adjuvant was a member of, and for not first identifying adjuvant by the full name before referring to them by the relevant abbreviation. The claim has been amended to correct these defects. The rejection is therefore withdrawn.

9. **(New Rejection- Necessitated by Amendment)** Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on a microparticle comprising an antigen adsorbed onto its surface wherein the antigen is derived from a pathogenic organism, wherein "said pathogenic antigen is a virus." There is no antecedent basis in the claims for the term antecedent antigen. However, there is basis for both the terms "pathogenic organism" and for antigens derived from such organisms. It is unclear from the claim whether the applicant intended to claim a microparticle where an entire virus is used as an antigen, or whether the claim was intended to read on microparticles comprising antigens derived from a virus.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. **(Prior Rejection-Withdrawn in part)** Claims 1, 4, 5, 7, 43, 45, 46, and 78 are rejected under 35 U.S.C. § 102(a) as being anticipated by Levy et al. In the prior action, claims 1-7, 11, 13, 14, 43-47, 54, 56, and 57 were rejected as being anticipated by Levy et al. (WO 96/20698). (It is noted that claim 55 was also rejected, however, that claim was cancelled in Amend. B.) These claims read generally on a microparticle comprising a polymer, a cationic or an anionic detergent, and an antigen, wherein the antigen comprises a polynucleotide (the elected invention). For the reasons stated below, the rejection is withdrawn as to the claims other than claims 1, 4, 5, 7, 43, 45, and 46, but is maintained as to those seven claims. Claim 78 is also anticipated by the reference for the same reasons as claim 4.

Levy teaches such a microparticle except that Levy also teaches that other detergents than anionic and cationic detergents may be used. In Amend. B, applicant argues that Levy does not teach the claimed invention. However, on pages 34-35, the reference teaches the making of a microparticle containing PVA, PLGA, and palmitic acid (disclosed as an anionic partitioning agent). Although palmitic acid is disclosed a “partitioning agent,” it does not appear that the use of the compound varies significantly from the use of the anionic detergents in the claimed invention. Thus, the reference teaches an embodiment of the claimed invention. The fact that the disclosed microparticle contains PVA does not destroy the anticipatory effect of the disclosure. This is because such inclusion is not excluded by either the open language of the claims (both claims 1 and 43 read “a microparticle *comprising*...”), or by the teachings of the specification. See e.g., page 3, lines 29-31 (stating “While particles made using only PVA may absorb some

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macromolecules, the microparticles of the present invention using other detergents alone, in combination, *or in combination with PVA*, adsorb a wide variety of macromolecules.” [italics added]). Thus, the reference anticipates at least claims 1, 4, 5, 7, 43, 45, 46, and 78. The rejection is thus maintained as to these claims for the reasons of record, and for the reasons discussed above.

However, the examiner agrees that the reference does not seem to directly anticipate the elected invention wherein the antigen is a nucleic acid. Thus, the rejection is withdrawn as to the claims other than claims 1, 4, 5, 7, 43, 45, 46, and 78. However, the examiner does find the reference applicable under 35 U.S.C. 103(a) as a reference rendering the claimed invention obvious. This rejection will be discussed more thoroughly below. The below discussion will also respond to those arguments set forth in Amend. B by the applicant intended to show non-obviousness.

In the traversal of the 102(a) rejection, the applicant also argues that the Levy reference is not enabling because the reference does not teach or suggest the claimed invention. See, Amend. B, page 13. However, in view of the above discussion, the teachings in Levy as to how to make the microparticles, the statements in the specification (page 6, lines 1921) that the methods disclosed in the present application are generally conventional and described in the literature, and the failure of the applicant to identify a claimed limitation that is not taught by the reference, the traversal is not found persuasive. The rejection is therefore maintained to the extent stated above.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. **(New Rejection)** Claims 1-7, 11, 13, 14, 43-47, 54, 56, 57, 75, 76, and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy et al. in view of Unger et al., U.S. Patent 5,830,430 or alternatively in view of Bertling et al., Biotech, and App. Biochem., 13:390-405. These claims were rejected in the prior action under 35 U.S.C. 102(a) as being anticipated by Levy et al. (WO 96/20698). These claims read generally on a microparticle comprising a polymer, a cationic or an anionic detergent, and an antigen, wherein the antigen comprises a polynucleotide (the elected invention). The rejection was withdrawn in part for the reasons provided above. Although the Levy reference anticipates claims 1, 4, 5, 7, 43, 45, and 78, it does not directly anticipate claims 2, 3, 6, 11, 13, 14, 44, 47, 54, 56, and 75, and 76. However, it does render the later claims obvious for the reasons of record. In combination, the references also render claims 16, and 17 obvious.

However, the applicant does appear to be correct in the argument that the Levy reference alone does not teach a preference or motivation to prefer anionic or cationic detergents to other detergents. Thus, the rejection is hereby restated as a rejection based on Levy in view of Unger or Bertling. Unger teaches that cationic agents are particularly useful for use as carriers of bioactive

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agents. Abstract. Among the forms that the cationic agents are able to take are spherical entities, which appears to include microspheres and microparticles. Columns 8-9. Further, the patent teaches that the cationic agents are preferably used with anionic bioactive agents, including proteins and polynucleotides. Columns 9, lines 43-65, and column 17, lines 6-46. The patent also suggests that the utility of the agents taught in the specification is due to their charge. Col. 17, lines 6-16. Bertling also teaches that the use of nanoparticles, and other bioagent carriers, to carry DNA may be improved by giving the particles a positive charge. See, abstract, and page 391. Thus, when either Bertling or Unger is read in combination with Levy, it would have been obvious to one of ordinary skill in the art to achieve better binding of polynucleotides in microparticles by using cationic detergents.

The references therefore render the use of cationic detergents to bind negatively charged bioactive agents obvious. Further, because the references teach the importance of the charge of the detergents to the improved ability to bind the bioactive agents, it would likewise have been obvious to those of ordinary skill in the art to use anionic detergents in the making of the microparticles where the antigen to be attached had a positive charge. The motivation to combine the references would be to improve the ability of the particles of Levy to bind bioactive agents. There would also have been a reasonable expectation of success because there is no reason to suspect that the incorporation of the cationic agents into the microparticles of Levy would be inoperative.

14. **(New Rejection)** Claims 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy in view of either Unger or Bertling as applied to claims 1-7, 11, 13, 14,

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43-47, 54, 56, 57, 75, 76, and 78 above above, and further in view of, respectively, U.S. Patent 5,630,922, issued to Eswarakrishnan et al. (the '922 patent), and U.S. Patent 4,534,996, issued to Rembaum et al. (Rembaum). These claims describe the claimed microparticle wherein the detergent is, respectively, the cationic detergent hexadecyltrimethylammonium bromide, or the anionic detergent sodium dodecyl sulfate. As described above, Levy in view of Unger and Bertling render obvious the use of charged surface adjusting particles to improve the binding of the microparticle to the bioactive agents. The '922 patent demonstrates that hexadecyltrimethylammonium bromide was a known cationic detergent useful in pharmaceutical compositions, including microparticles. See, cols. 8-9. The compound was known to be cationic. See e.g. U.S. Patent 5,714,354, col. 3, lines 44-46. Rembaum likewise demonstrates that sodium dodecyl sulfate was a known anionic detergent useful in microparticle compositions. See, col. 5, lines 28-33. Because these compounds were known both as usable in pharmaceutical microparticles, and for their ionic characteristics, it would have been obvious to one of ordinary skill in the art to use these compounds in the microparticles suggested by the Levy in view of Unger.

15. **(New Rejection-Necessitated by Amendment)** Claims 69-74, 79, 80, and 85-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy in view of Unger or alternatively in view of Bertling as applied to claims 1-7, 11, 13, 14, 43-47, 54, 56, 57, 75, 76, and 78 above.

Claim 69 of the present invention describes the microparticle of claim 1 where the antigen is not entrapped within the microparticle. Levy further discloses that the polymeric core of the nanoparticles may have bioactive agents in the core of the polymer matrix. Thus, the

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reference is clearly teaching that such an inclusion is optional, thereby rendering obvious embodiments where the antigens are only on the surface of the particle.

Claim 70 requires that the claimed microparticle be made by a method of double emulsion. The applicant discloses in the specification that this is a known method for making microparticles. Page 18, lines 10-15. Further, Levy discloses that single or multiple emulsion methods may be used to make the microparticles disclosed therein. It would therefore have been obvious to one of ordinary skill in the art to use a known method of making microparticles to make the particles suggested by Levy in combination with Unger or Bertling.

Claims 71-74 describe microparticles wherein the antigen is derived from, respectively, a pathogenic organism, a pathogenic bacterium, a pathogenic virus, and a microparticle where the antigen is one of several targeting specific organisms. These claims are all rendered obvious by the above references as Levy teaches that the microparticle disclosed therein may comprise an protein vaccine from tetanus, pertussis, or other bacteria, AIDS antigens, influenza virus antigens, hepatitis viral antigens, and other viral antigens. Pages 10-11. In the same sentence, the patent indicates that DNA vaccines to the same organisms may be used. *Id.* Thus, Levy in view of Unger or Bertling also render claims 71-74 obvious. Further, as all of the antigens suggested in claim 74 are known in the art, it would likewise be obvious to one of ordinary skill in the art to use any of them, even those not specifically disclosed in the cited references, in the disclosed microparticles.

Claims 79, 80, and 85-90 describe compositions of the claimed microparticle with a pharmaceutically acceptable excipient, and compositions that may be injected. Levy suggests the

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production of injectable microparticle compositions, as well as formulations for other administration routes. Pages 25-26. It would therefore have been obvious to one of ordinary skill in the art to make the microparticles suggested by Levy in view of Bertling or Unger, and to make compositions of the particles in combination with pharmaceutical excipients, including those rendering the composition acceptable for injection.

16. **(Prior Rejections- Reformulated)** Claim 10, or claims 10, 12, and 15 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable respectively over Levy further in view of Moore and Haynes, and Levy in view of Cleland. Claims 16, 58, and 59 were also rejected over Levy in view of either Moore and Haynes, or of Cleland, and, respectively, further in view of Cox, Carlo, and Macfarlane. The only traversal made with regards to these rejections was that Levy alone did not teach or render obvious either claims 1 or 43. In view of the above discussions, the rejections are maintained over Levy in view of either Bertling or Unger as described above, further in view of the relevant other references for the reasons of record.

17. **(New Rejection- Necessitated by Amendment)** Claim 77 is rejected under 35 U.S.C. 103(a) as being unpatentable over Levy in view of either Unger or Bertling as applied to claims 1-7, 11, 13, 14, 43-47, 54, 56, 57, 75, 76, and 78 above, and further in view of Hedley et al. (of record in the IDS filed September 30, 2002). This patent teaches microparticles for the delivery of nucleic acids that are made and used in similar ways to the nanoparticles of Levy. In the description of how to make the desired microparticles, the patent teaches a method that resulted in particle of between 1.1 and 10 μ m. Column 14, lines 8-54. The purpose of both the

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Levy and Hedley particles are similar. However, because the purpose of the Hedley patent was to make particles specifically for nucleic acid delivery, it would have been obvious to one of ordinary skill in the art to make the particles with the components disclosed by Levy and Unger or Bertling using the method disclosed by Hedley. It would therefore have been obvious to one of ordinary skill in the art to make a particle of between 500nm and 10 μ m.

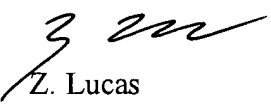
Conclusion

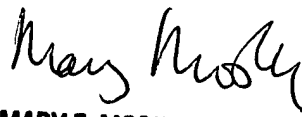
18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
December 4, 2002


MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
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